REMARKS

The Official Action of March 31, 2003 has been carefully considered. Applicants appreciate the Examiner's thorough review of the application. The changes presented herewith, taken with the following remarks, are believed sufficient to place the present application in condition for allowance. Reconsideration is respectfully requested.

By the present amendment, claims 22-24 have been amended without changing the scope of the claims and new claims 103-124 have been added. Support for claims 103 and 104 can be found in original claims 24 and 25 respectively. Support for claims 105-107 and 112-114, for example, can be found in FIG. 4 and in the specification on page 24, line 21 through page 25, line 19. Support for claims 109, 116, 118 and 123 can be found in original claim 23. Support for claims 110 and 119 can be found in original claim 26. Support for claims 111, 120 and 124 can be found in original claim 27. New independent claims 115, 117 and 122 include limitations from original claim 21. Claim 117 also includes limitations from original dependent claim 22. Claim 122 also includes limitations from original dependent claim 26. The amendments and additional claims are not believed to involve the introduction of new matter. Accordingly, claims 21-27 and 103-124 stand pending in this application and are believed to be in condition for allowance.

In the Official Action, the Examiner rejects claim 21-27 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,435,076 to Hjertman et al. in view of U.S. Patent No. 5,184,450 to Galy et al. or U.S. Patent No. 4,941,876 to Meyer et al. Applicants respectfully traverse this rejection.

Claim 21 sets forth a process for the manufacture of a prefilled syringe type ampoule including the steps of inserting a piston through a front end opening of a barrel to a distance from the front end opening into a sealing engagement with the barrel interior to form a chamber between the piston and the front end opening. The process further includes the steps of filling material into the chamber by passing the material through the front end opening and sealing the front end opening with the sealer.

Hjertman discloses a process of manufacturing injection cartridges of the dual-chamber type (see column 6, starting at line 48). The Hjertman process includes the step of inserting a movable wall (3) to a predetermined position in relation to a bypass arrangement (4). The front chamber (5) of the cartridge is then filled with a predetermined amount of a solution, and the filled cartridge is placed with the front opening upwards in a suitable tray for freeze-drying. As described in column 7 of Hjertman, an arrangement of cartridges and sleeves with stoppers are introduced into a freeze-drying apparatus and the freeze-drying procedure is carried out. After freeze drying, the front chambers of the cartridges are sealed by inserting the stoppers (11) in the necks (2) of the cartridges. Once the front chambers of the cartridges have been sealed, the cartridges are taken out from the freeze-drying apparatus, and the liquid component is filled into the cartridges through their rear ends, which are subsequently closed by means of the pistons (25).

Hjertman, however, does not appear to teach or suggest an ampule barrel with a substantially constant cross-section between a front end and a rear end nor the step of inserting the piston through the front end opening as recited in claim 21. The description portion of the specification specifically points out that the claimed manufacturing process of the present

application provides improvements over the cited Hjertman reference. For example, the present invention provides improvements with respect to the manufacture of ampoules in highly automated processes (see page 2, line 26 through page 3, line 7; in particular page 3, lines 6-7). In addition, the specification of the instant application also states that the present invention further facilitates filling operations through the front opening and allows a piston to be inserted through the front opening and not only through the rear opening, which may be used to reduce necessary manufacturing steps and facilitate equipment design by allowing more steps to be conducted from the same side (see page 3, lines 27-31). Indeed, page 25, lines 12-14 describes the process, with reference to FIG. 4, wherein all of the steps up to step (46) inclusive can be conducted from the upper side of the carrier. Therefore, clear advantages are achieved with a process for the manufacture of a prefilled syringe type ampoule including the steps of inserting a piston through the front end opening of a barrel, filling material into the chamber by passing the material through the front end opening and sealing the front end opening with a sealer as set forth in claim 21.

In the Official Action dated March 31, 2003, the Examiner states that Hjertman does not disclose how the first piston is inserted into the barrel. The Examiner states that Galy and Meyer show the insertion of a piston/moveable plug 9 and 25, respectively, and filling material through the same end of the ampoule since the diameter of the ampoule is constant. Consequently, it is the Examiner's position that it would have been obvious to insert the piston and material of Hjertman through the same front opening since, allegedly, the diameter of the Hjertman piston is the same diameter of the ampoule. Applicant respectively traverses this assertion.

Hjertman provides no teaching of a process as presently claimed wherein both a piston and filling material are provided through a front end opening of a barrel. Moreover, the teachings of Hjertman would not render such a process obvious to one of ordinary skill in the art.

The Examiner asserts that Hjertman discloses an ampoule barrel with a substantially constant cross-section like Galy and Meyer. However, as set forth below, Applicants submit that Hjertman does not teach or suggest a barrel having substantially constant cross-section between the front end and the rear end to one of ordinary skill in the art. Indeed, Hjertman states throughout the application that the invention is directed to a dual-chamber type injection cartridge (See Column 1, lines 8-9 and 67; Column 2, lines 20-22 and 39-42; Column 3, lines 25-26, 27-28 and 38-41; Column 6, lines 47-51; and Column 7, lines 56-61). The dual chamber cartridge includes a front chamber (5) that can be isolated from a rear chamber (6) by a movable wall (3). The front chamber (5) is designed to contain a solution (18, see FIG. 1) that is converted into a solid component (19, see FIG. 2) after a freeze-drying process. The rear chamber (6) can also be filled with a liquid component (See FIG. 4) for later mixing with the solid component (19).

It is believed that Hjertman only teaches dual-chamber cartridges with a barrel of the shape depicted in FIG. 2, a highlighted copy of which appears in Illustration A below.

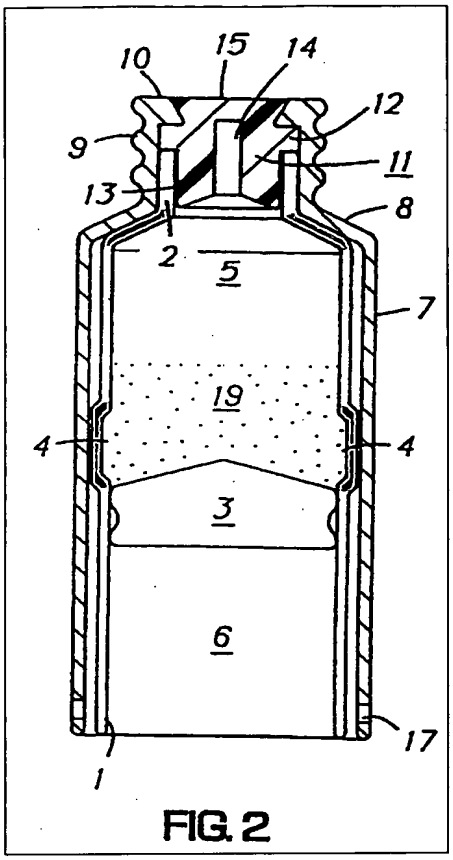

FIG. 2

Illustration A

As shown in Illustration A, the barrel appears in yellow, green, blue and pink highlighted portions. The barrel receives a movable wall (3) having an outer diameter being approximately equal to the interior diameter of the yellow highlighted portion. It is noted that the movable wall (3) is located below a bypass wall portion highlighted in green to permit mixing of the solid component (19) with liquid in the rear chamber (6) at the desired time. The front end of the barrel includes a neck portion (2), highlighted in pink, that is connected to the yellow highlighted portion with a transition portion highlighted in blue. The neck portion (2) has a substantially smaller diameter than the outer diameter of the movable wall (3).

It is believed that FIG. 3 of Hjertman also teaches an embodiment of a dual-chamber cartridge with a barrel of the general shape depicted in FIG. 2 found in Illustration A above, and that any barrel features of FIG. 2 which are omitted from FIG. 3 are impliedly included to permit the cartridge to function in a manner consistent with the remaining teaching of Hjertman. More specifically, a highlighted copy of FIG. 3 appears in Illustration B below.

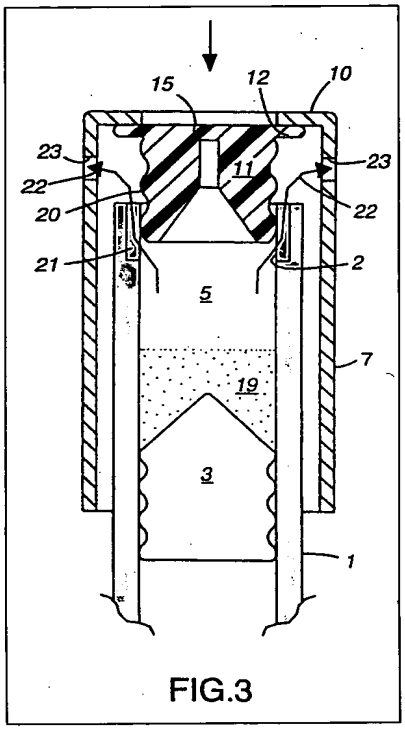

FIG.3

Illustration B

The orange highlighted portion of the barrel depicted in Illustration B is believed to be only a general depiction of the more specifically described highlighted blue, yellow, pink and green barrel portions in Illustration A above, as Hjertman provides no other teaching or description of a cartridge barrel without a bypass as shown in FIG. 2 and required for operation of a dual-

chamber device, or without a narrowed neck as shown in FIG. 2. Thus, the orange highlighted portion of the barrel is only a general illustration of the actual barrel shape as more specifically described in FIG. 2.

The written portion of the specification (i.e., column 4, lines 25-42) further supports the position that the orange highlighted portions of Illustration B are a general representation of the more specific barrel shape shown in Illustration A above. The specification implies the modification of the device shown in FIG. 3 only includes changes to the stopper arrangement when stating that "FIG. 3 shows, in a somewhat larger scale, a modification of the stopper arrangement." (Column 4, lines 25-26). Therefore, the differences are focused on the stopper (11), the sealing ridges (20), and potentially the cooperating purple highlighted portions of the barrel referenced at (21). Other than the highlighted purple areas in FIG. 3, the remaining shape of the barrel does not appear to have any functional relationship to the modified stopper arrangement. Accordingly, all embodiments of the Hjertman barrel, including the barrel generally depicted in FIG. 3, have the same shape with a neck portion (2) including a substantially smaller diameter than the outer diameter of the movable wall (3) as shown in Illustration A above.

As the neck portion (2) has a substantially smaller diameter than the outer diameter of the movable wall (3), as specifically shown in FIG. 2 and not contradicted by the general disclosure of FIG. 3, Hjertman teaches away from insertion of a piston through the front end opening as required by claim 21. In addition, the frustoconical taper of the movable wall (3), shown in FIG. 3, is also pointing toward the front end opening of the barrel, which would

typically indicate to one of ordinary skill in the art that the movable wall is being inserted from the rear end.

Moreover, the deficiencies of Hjertman are not resolved by Galy or Meyer. Galy fails to provide any teaching or suggestion to insert the piston through the front end opening as required by claim 21. Rather Galy discloses insertion of a plug (9) through the rear end of the body (See FIG. 9b of Galy). Galy, therefore, cannot provide any suggestion or motivation to insert the Hjertman piston through the front end opening of the barrel. Similarly, Meyer fails to provide any teaching or suggestion to insert the piston of Hjertman through the front end opening as required by claim 21. Meyer discloses a closed end ampoule (10) wherein a liquid substance (27') is first introduced into the ampoule (10) as illustrated in FIG. 2. Following lyophilization, the liquid substance (27') is transformed into lyophilisate (27) and a plug (25) is then inserted into the ampoule (10) after which liquid solvent (28) is introduced as shown in FIG. 6. Meyer et al., therefore discloses a process of forming an ampoule (10) wherein the ampoule has a closed end and lyophilizate is trapped at the closed end.

In contrast, Hjertman does not disclose a closed-ended barrel but discloses a barrel having open opposed ends. As described in Column 6, lines 52-62 of Hjertman, the movable wall (3) is first inserted to a predetermined position in relation to the bypass arrangement (4). Next, the front chamber (5) is apparently filled with a predetermined amount of a solution (18) through the open front end then freeze-dried into the solid component (19). The rear chamber (6) is then apparently filled with liquid through the opposite open rear end. Accordingly, Meyer involves a different process of fabricating an ampoule using a closed ended barrel while Hjertman discloses filling of liquid solution through both open ends of a barrel. Meyer

therefore cannot provide a motivation to insert the movable wall of Hjertman through the front end opening at the neck of Hjertman.

Hjertman in view of either Galy or Meyer fail to render obvious the further limitations of claim 24 which recites connecting the front part of the sleeve to the sealer after the step of sealing the front end opening with the sealer. Hjertman discloses a sleeve (7) attached to the stopper (11) prior to sealing the front end of the opening with the stopper (see FIGS. 1 and 2). Galy apparently fails to disclose any sleeve and therefore cannot provide a motivation to modify the attachment of the sleeve of Hjertman. Furthermore, Meyer discloses an injector (11) including a capsule (15) and stopper means (19) that appear connected together as a unit (see column 4, lines 52-63). Accordingly, Meyer cannot provide a motivation to modify the attachment of the sleeve of Hjertman.

Thus, the processes defined by claims 21-27 are nonobvious over and patentably distinguishable from Hjertman in view of Galy or Meyer, whereby the rejection under 25 U.S.C. § 103 has been overcome. For the reasons stated above, Applicant respectfully requests allowance of claim 21. Applicant further requests allowance of claims 22-27 since these claims depend directly or indirectly from allowable independent claim 21. Claims 103-124 have been added to provide additional claim scope and are believed to be in condition for allowance.

It is believed that the above represents a complete response to the outstanding Office action. Reconsideration and early allowance are respectfully requested.

Respectfully submitted,

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